Study Protocol and Statistical Analysis Plan

Comparison of Surgical Outcomes and Accommodative Changes in Patients With Primary Exotropia Undergoing Medial Rectus Resection-Lateral Rectus Recession and Medial Rectus Plication-Lateral Rectus Recession

Brief Title: Accommodative Changes After Medial Rectus Resection Versus Plication in Primary Exotropia

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1. Study Synopsis

Study Design	Prospective, interventional, non-randomized, parallel-group comparative clinical study.
Population	Patients aged 5 to 40 years with basic primary exotropia eligible for unilateral horizontal strabismus surgery.
Study Period	February 2024 to July 2025.
Setting	Department of Ophthalmology, Basaksehir Cam and Sakura City Hospital, University of Health Sciences.
Allocation	Alternating sequential allocation according to enrollment order; no randomization procedure was used.
Intervention Arms	1) Lateral rectus recession plus medial rectus resection (LRR+MRR). 2) Lateral rectus recession plus medial rectus plication (LRR+MRP).
Planned Sample Size	At least 36 patients per group to account for possible loss to follow-up.
Final Analysis Population	85 patients: 40 in the LRR+MRR group and 45 in the LRR+MRP group.
Primary Outcome	Change in accommodative amplitude from baseline to postoperative follow-up.
Secondary Outcomes	Ocular alignment and surgical success.
Follow-up Visits	Postoperative week 1, postoperative month 1, and postoperative month 3.
Statistical Software	IBM SPSS Statistics version 28.0.

2. Background and Rationale

Primary exotropia is a form of horizontal strabismus characterized by outward deviation of one eye. Surgical correction is considered when the deviation is clinically significant, stable, symptomatic, cosmetically concerning, or associated with impaired binocular function. Horizontal strabismus surgery commonly combines weakening of the lateral rectus muscle and strengthening of the medial rectus muscle.

Medial rectus resection has traditionally been used as a strengthening procedure. Medial rectus plication is an alternative strengthening technique in which the muscle is folded and sutured without complete disinsertion from its scleral insertion. Plication may preserve anterior ciliary vessels and adjacent neurovascular structures more effectively than resection. Because the anterior ciliary arteries and related neural pathways contribute to anterior segment physiology and ciliary muscle function, the surgical technique may influence postoperative accommodation.

The purpose of this study is to compare medial rectus resection and medial rectus plication, each combined with lateral rectus recession, with respect to postoperative accommodative changes and surgical outcomes in patients with primary exotropia.

3. Objectives

3.1 Primary Objective

To compare postoperative changes in accommodative amplitude between patients undergoing unilateral lateral rectus recession combined with medial rectus resection and those undergoing unilateral lateral rectus recession combined with medial rectus plication.

3.2 Secondary Objectives

- To compare postoperative ocular alignment between the two surgical groups.
- To compare surgical success at postoperative month 3 between the two surgical groups.
- To evaluate time-dependent changes in accommodative amplitude during postoperative follow-up.

4. Study Design

This is a prospective, interventional, non-randomized, parallel-group comparative clinical study conducted at a single tertiary ophthalmology center. Participants with primary exotropia were assigned to one of two surgical groups. The study compared unilateral lateral rectus recession plus medial rectus resection with unilateral lateral rectus recession plus medial rectus plication.

Participants were allocated using an alternating sequential allocation method according to the order of enrollment. The first participant who consented to participate was assigned to the LRR+MRR group, the second participant was assigned to the LRR+MRP group, and subsequent participants were assigned alternately thereafter. No random sequence generation, allocation concealment, or randomization procedure was used.

5. Study Population

5.1 Inclusion Criteria

- Patients aged 5 to 40 years.
- Diagnosis of basic primary exotropia.
- Stable deviation angle over three consecutive preoperative visits.
- Deviation angle of at least 20 prism diopters.
- Literacy and cooperation sufficient to perform accommodative amplitude testing.
- Agreement to undergo unilateral horizontal strabismus surgery.
- Written informed consent obtained from the participant and/or legal guardian.

5.2 Exclusion Criteria

- Spherical refractive error greater than +/-5.00 diopters.
- Cylindrical refractive error greater than +/-3.50 diopters.
- Best-corrected visual acuity worse than 0.1 logMAR.
- Paralytic or restrictive strabismus.
- Previous strabismus surgery.
- Additional ocular pathology, including glaucoma, cataract, uveitis, scleritis, retinal disease, macular disease, or optic neuropathy.
- History of ocular trauma.
- Axial length greater than 26.5 mm.
- Aphakia or pseudophakia.
- High accommodative convergence/accommodation ratio.
- Presence of systemic disease.
- Use of medications known to affect accommodation, including topical pilocarpine, cycloplegics, tricyclic antidepressants, or anticholinergic agents.
- Incomplete ophthalmologic or accommodative examinations.
- Loss to follow-up.

6. Interventions

6.1 Lateral Rectus Recession Plus Medial Rectus Resection

Participants in this arm underwent unilateral horizontal strabismus surgery consisting of lateral rectus recession combined with medial rectus resection. The lateral rectus muscle was weakened by recession, and the medial rectus muscle was strengthened by resection. In the resection procedure, the medial rectus muscle was isolated, disinserted, shortened by removing a measured segment according to the planned

surgical dosage, and reattached to the sclera. Surgical dosage was determined according to the preoperative distance deviation angle.

6.2 Lateral Rectus Recession Plus Medial Rectus Plication

Participants in this arm underwent unilateral horizontal strabismus surgery consisting of lateral rectus recession combined with medial rectus plication. The lateral rectus muscle was weakened by recession, and the medial rectus muscle was strengthened by plication. In the plication procedure, the medial rectus muscle was folded and sutured to strengthen the muscle without complete disinsertion from its original scleral insertion. Surgical dosage was determined according to the preoperative distance deviation angle.

6.3 Operative and Postoperative Management

All procedures were planned and performed under general anesthesia by an experienced strabismus surgeon. Postoperative topical moxifloxacin-dexamethasone drops were prescribed and tapered over one month. Postoperative follow-up examinations were performed at week 1, month 1, and month 3.

7. Study Assessments

7.1 Preoperative Ophthalmologic and Strabismus Examination

All participants underwent comprehensive ophthalmologic examination, including cycloplegic refraction, best-corrected visual acuity assessment, slit-lamp examination, dilated fundus examination, axial length measurement, and ocular motility assessment. Distance and near deviation angles were measured in primary position using the prism and alternate cover test, with and without spectacles, on at least three preoperative visits. Refractive data were converted to spherical equivalent. Near deviation was repeated with a +3.00 diopter lens to assess for a high accommodative convergence/accommodation ratio.

7.2 Measurement of Accommodative Amplitude

Accommodative amplitude was measured separately in each eye using the minus lens method by a single investigator. Measurements were performed in a well-lit room with the participant seated comfortably. Participants wore their distance correction when needed, and the fellow eye was occluded during monocular testing. A near acuity chart was held at 33 cm, and participants were asked to read the smallest visible line. Minus lenses were added over the distance correction in 0.25-diopter increments until the target could no longer be read clearly. The highest minus lens power at which clear near vision was maintained was recorded, and 3.00 diopters were added to account for the 33-cm working distance.

7.3 Postoperative Follow-up

Follow-up examinations were performed at postoperative week 1, postoperative month 1, and postoperative month 3. At each visit, best-corrected visual acuity, ocular motility, primary position deviation angle, and accommodative amplitude were recorded.

8. Outcome Measures

8.1 Primary Outcome Measure

Change in accommodative amplitude: Accommodative amplitude was measured separately in each eye using the minus lens method. Measurements were performed before surgery and at postoperative week 1, postoperative month 1, and postoperative month 3. Changes were calculated by comparing postoperative values with the baseline preoperative value and were recorded in diopters.

8.2 Secondary Outcome Measures

- Ocular alignment: Ocular deviation in primary position was measured using the prism and alternate cover test. Distance and near deviation angles were recorded in prism diopters at baseline and during postoperative follow-up.

- Surgical success: Surgical success was assessed at postoperative month 3 and was defined as ocular deviation in primary position of 10 prism diopters or less of exotropia or 5 prism diopters or less of esotropia.

9. Sample Size

A prior sample size calculation was performed based on the expected between-group difference in operated-eye change in accommodative amplitude from baseline to postoperative week 1, which was considered the primary functional outcome for sample size planning. Assuming a two-sided alpha level of 0.05, 80% power, an anticipated mean difference of 0.7 diopters, and a common standard deviation of 0.97 diopters, the minimum required sample size was estimated to be 31 patients per group. To allow for possible loss to follow-up, at least 36 patients were considered necessary in each group. The final analysis included 85 patients: 40 in the LRR+MRR group and 45 in the LRR+MRP group.

10. Statistical Analysis Plan

All statistical analyses will be performed using IBM SPSS Statistics version 28.0. Continuous variables will be assessed for normality using the Shapiro-Wilk test. Normally distributed continuous variables will be presented as mean +/- standard deviation. Non-normally distributed continuous variables will be presented as median and range. Categorical variables will be presented as number and percentage.

Between-group comparisons of continuous variables will be performed using the Mann-Whitney U test when variables are not normally distributed. Comparisons among more than two independent groups will be performed using the Kruskal-Wallis test. Repeated measurements within groups will be analyzed using the Friedman test. When significant differences are identified in repeated-measure analyses, pairwise comparisons will be performed using the Wilcoxon signed-rank test with Bonferroni correction.

Associations between categorical variables will be evaluated using the Pearson chi-square test or Fisher exact test, as appropriate. A two-sided p value less than 0.05 will be considered statistically significant.

The main comparative analysis will evaluate postoperative changes in accommodative amplitude within and between the LRR+MRR and LRR+MRP groups. Secondary analyses will compare ocular alignment and surgical success between groups. Age-stratified analyses may be performed using predefined age categories of 5-12 years, 13-19 years, and 20-40 years, with delta accommodative amplitude used to minimize the effect of age-related baseline differences in accommodation.

11. Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of Basaksehir Cam and Sakura City Hospital. Written informed consent was obtained from all participants and/or their legal guardians before enrollment. Participation did not change the standard clinical indication for surgery, and both surgical techniques are established procedures used in the management of horizontal strabismus.

12. Data Management and Confidentiality

Study data were collected from ophthalmologic examinations and postoperative follow-up assessments. Data were recorded in a deidentified research dataset for analysis. No names, direct identifiers, or individual participant identifiers are included in this public protocol document.

13. Individual Participant Data Sharing Statement

Individual participant data will not be shared because no specific data-sharing plan was included in the study protocol or informed consent documents.

14. Safety Considerations

Both interventions are standard surgical procedures for horizontal strabismus. Postoperative clinical assessments included best-corrected visual acuity, ocular motility, ocular alignment, and clinical examination. Patients requiring further management after completion of the study follow-up were treated according to routine clinical practice. Patients with residual exotropia of 12 prism diopters or more at postoperative month 3 were scheduled for additional surgery in the fellow eye after completion of the study follow-up period.